



[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The invention listed below is jointly owned by an agency of the U.S. Government with Vanderbilt University, University of Alabama and University of Pennsylvania and is available for licensing to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION CONTACT: Licensing information and copies of the U.S. patent application listed below may be obtained by communicating with Sury Vepa, Ph.D., J.D., Senior Licensing and Patenting Manager, National Center for Advancing Translational Sciences, NIH, 9800 Medical Center Drive, Rockville, MD 20850, Phone: 301-827-7181, or email sury.vepa@nih.gov. A signed Confidential

Disclosure Agreement will be required to receive copies of unpublished patent applications.

SUPPLEMENTARY INFORMATION: Technology description follows.

Thiazole Based Inhibitors of Lactate Dehydrogenase (LDH) for the Treatment of Cancer

Description of Technology:

Agents that target enzymes involved in cancer cell metabolism offer an attractive therapeutic route in view of the potential to preferentially target cancer tissue over normal tissue. While normal tissue typically uses glycolysis as a major cellular metabolic path only when the oxygen supply is low, cancer tissue relies heavily on aerobic glycolysis regardless of the oxygen supply level. In addition, metabolic switching to a more glycolytic phenotype is a required step with inflammatory cells and other pathologies which require activated glycolysis in their metabolism. Lactate dehydrogenase (LDH) is involved in the final step of glycolysis, in which pyruvate is converted to lactate and the conversion of NADH to NAD⁺. There are two different genes of LDH, LDHA and LDHB, but both proteins (subunits) have the same active site and catalyze the conversion of pyruvate to lactate or lactate to pyruvate. In cancer patients, serum total lactate dehydrogenase levels are often increased, and the gene for LDH is up-regulated. LDH inhibition is expected to reduce the ability of the cell to effectively metabolize glucose and reduce tumor cell proliferation and tumor growth and other pathologies which involve a glycolytic metabolic switch. Thus, compounds that inhibit LDH activity have potential for the development of anti-cancer therapeutics. Previously developed LDH inhibitors have significant drawbacks, including poor potency and/or poor bioavailability,

limiting their utility as therapeutics. The present technology provides novel 1 H-PYRAZOL-1 -YL-THIAZOLE based LDH inhibitors with improved potency, selectivity, and/or bioavailability for the treatment of cancer.

This technology is available for licensing for commercial development in accordance with 35 U.S.C. § 209 and 37 CFR Part 404, as well as for further development and evaluation under a research collaboration.

Potential Commercial Applications:

- Novel therapeutics for cancer AND indications which depend on a metabolic switch to glycolysis (e.g., inflammation, autoimmune disease, etc.)

Competitive Advantages:

- Novel LDH inhibitors with improved potency, selectivity, and/or bioavailability for the treatment of cancer.

Development Stage:

- Optimized lactate dehydrogenase inhibitors are in pre-clinical development

Inventors:

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Publications: This manuscript reports early compounds in the series:

<https://pubs.acs.org/doi/10.1021/acs.jmedchem.7b00941>

Intellectual Property: 1. SMALL MOLECULE INHIBITORS OF LACTATE DEHYDROGENASE AND METHODS OF USE THERE OF, PCT/US2015/067895 filed on December 29, 2015 and published as WO 2016/109559 on July 7, 2016 (HHS Ref. No. E-244-2014), and

2. 1 H-PYRAZOL-1 -YL-THIAZOLES AS INHIBITORS OF LACTATE DEHYDROGENASE AND METHODS OF USE THERE OF, PCP/US2017/040021 filed on June 29, 2017 and published as WO 2018/005807 on January 8, 2018 9HHS Ref. No. E-190-2016).

Related Intellectual Property: HHS Reference Number E-293-2011.

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Dated: July 5, 2018.

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